Affinity-based profiling of the adenosine receptors

Beerkens, B.L.H.

Citation
Beerkens, B. L. H. (2023, November 9). *Affinity-based profiling of the adenosine receptors*. Retrieved from https://hdl.handle.net/1887/3656497

Version:	Publisher's Version
License:	Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden
Downloaded from:	https://hdl.handle.net/1887/3656497

Note: To cite this publication please use the final published version (if applicable).

Stellingen

Behorende bij het proefschrift

Affinity-Based Profiling of the Adenosine Receptors

1. Chemical probes can aid the detection of GPCRs and thereby offer new possibilities to study GPCRs on a molecular level.
   This thesis, chapters 2-7

2. Non-specific reactivity should always be kept in mind when implementing electrophilic groups in the design of chemical probes. However, ensuring a high affinity towards the protein target of interest is a good way to reduce and sometimes even overcome unwanted side reactions.
   This thesis, chapters 2-6

3. Introduction of a ‘click handle’ onto the right position of an existing covalent ligand results in a versatile probe molecule that can be used in a wide range of biochemical assay types.
   This thesis, chapters 2, 4-6

4. Chemical pull-down proteomics is a promising example of a biochemical assay type that benefits from the aid of chemical probes to perform measurements on lowly abundant GPCRs.
   This thesis, chapter 4

5. Detectable off-target protein labeling does not necessarily hinder proper detection and analyses of the protein target of interest. Choosing the wrong conditions does.
   This thesis, chapters 4-6

6. New paradigms regarding GPCR signaling, such as biased, oligomeric and compartmentalized signaling, expand the opportunities for therapeutic interventions. The development of new chemical biology tools is absolutely required to understand these forms of noncanonical GPCR regulation.
   Adapted from M.M. Shchepinova, E.W. Tate, et al. Curr. Opin. Chem. Biol. 2020

7. Despite having multiple beneficial properties as compared to antibodies, small molecular probes are still underappreciated tools to target and detect GPCRs.

8. Correct usage of chemical probes needs to be promoted effectively from medicinal chemist to biologist, up to clinical researcher.
   Adapted from J. Sterling, L. Munoz, et al. Nat Commun, 14, 2023

9. Synthesizing new molecules is fun, but not always the answer to your problems.

10. Sustainability should be taken more seriously at places where tremendous amounts of chemicals and disposables are being used.

Bert Beerkens
Leiden, 9 November 2023